

Appl. No. 09/980,564
Amdt. dated May 19, 2005

PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-120. (Canceled)

121. (Currently amended) A recombinant, double-stranded, adenovirus vector comprising a parallel DNA strand and an anti-parallel DNA strand, wherein the vector parallel strand comprises:

- a. an adenovirus left inverted terminal repeat sequence;
- b. an adenovirus packaging sequence;
- c. a first adenoviral-associated inverted terminal repeat sequence;
- d. a first inverted repeat sequence;
- e. a heterologous promoter sequence which mediates transcription in a direction towards the adenoviral left inverted terminal repeat sequence in part step a;
- f. a foreign gene sequence;
- g. a second inverted repeat sequence;
- h. a second adenoviral-associated inverted terminal repeat sequence;
- i. a nucleotide sequence that mediates replication of an adenovirus in a transduced cell; and
- j. an adenovirus right inverted terminal repeat sequence;

wherein the adenovirus packaging sequence is located on the parallel strand of the vector; and wherein the anti-parallel strand comprises a nucleotide sequence encoding a modified adenoviral fiber protein which alters the tropism of the adenovirus vector, and

wherein the modified adenoviral fiber protein is a modified fiber knob, a modified fiber tail or a modified fiber shaft.

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122. (Currently amended) A recombinant, double-stranded, adenovirus vector comprising a parallel and an anti-parallel DNA strand, wherein the vector parallel strand comprises:

- a. an adenovirus left inverted terminal repeat sequence;
- b. an adenovirus packaging sequence;
- c. a first adenoviral-associated inverted terminal repeat sequence;
- d. a first inverted repeat sequence;
- e. a heterologous promoter sequence which mediates transcription in a direction away from the adenoviral left inverted terminal repeat sequence in part step a;
- f. a foreign gene sequence;
- g. a second inverted repeat sequence;
- h. a second adenoviral-associated inverted terminal repeat sequence;
- i. a nucleotide sequence that mediates replication of an adenovirus in a transduced cell; and
- j. an adenovirus right inverted terminal repeat sequence;

wherein the adenovirus packaging sequence is located on the parallel strand of the vector; and wherein the anti-parallel strand comprises a nucleotide sequence encoding a modified adenoviral fiber protein which alters the tropism of the adenovirus vector, and wherein the modified adenoviral fiber protein is a modified fiber knob, a modified fiber tail or a modified fiber shaft.

123. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber knob, the modified fiber tail or the modified fiber shaft is from an adenoviral serotype that differs from the serotype of the left or right adenoviral inverted terminal repeat sequence.

124. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber knob, the modified fiber tail or the modified fiber shaft is from adenoviral serotypes Ad3, Ad7, Ad9, Ad11 or Ad35.

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125. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber knob binds a cell surface protein on a target cell of interest.

126. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber knob is modified in the G-H loop region or H-I loop region.

127. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber knob comprises a heterologous peptide ligand which replaces the G-H loop region or H-I loop region.

128. (Previously presented) The adenoviral vector of claim 127, wherein the heterologous peptide ligand is an RI or RII protein from malaria circumsporozoite surface protein (CS).

129. (Previously presented) The adenoviral vector of claim 128, wherein the RI protein from malaria circumsporozoite surface protein (CS) comprises the amino acid sequence KLKQPG (SEQ ID NO.:12).

130. (Previously presented) The adenoviral vector of claim 128, wherein the RII protein from malaria circumsporozoite surface protein (CS) comprises the amino acid sequence EWSPCSVTCGNGIQVRIK (SEQ ID NO.:13).

131. (Previously presented) The adenoviral vector of claim 127, wherein the heterologous peptide ligand comprises the amino acid sequence:

- a. LGGKPDQ (SEQ ID NO.:15);
- b. LNGCGSC (SEQ ID NO.:16);
- c. LNGCGSGC (SEQ ID NO.:17); or
- d. LNGCGXXXXXXXXXXGC (SEQ ID NO.:18).

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132. (Previously presented) The adenoviral vector of claim 121 or 122 which infects hepatocytes, bone marrow cells, stem cells or breast cancer cells.

133. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the modified fiber shaft has a shortened length.

134. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the adenoviral packaging sequence and the left and right adenoviral inverted terminal repeat sequences are from the same adenoviral serotype.

135. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the adenoviral packaging sequence and the left and right adenoviral inverted repeat sequences are from serotype Ad5.

136. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the foreign gene sequence encodes a therapeutic gene product, a selectable gene product, or a reporter gene product.

137. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the therapeutic gene product is gamma globin or human alpha-1 antitrypsin.

138. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the selectable gene product is neomycin, ampicillin, penicillin, tetracycline or gentamycin.

139. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the reporter gene product is green fluorescent protein, beta galactosidase or alkaline phosphatase.

140. (Previously presented) The adenoviral vector of claim 121 or 122, further comprising an insulator element sequence.

141. (Previously presented) The adenoviral vector of claim 121 or 122, further comprising a bacterial origin of replication.

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142. (Previously presented) The adenoviral vector of claim 121 or 122, further comprising a nucleotide sequence encoding a rep78 protein.

143. (Currently amended) The adenoviral vector of claim 121 or 122, wherein the gene sequence that mediates replication of an adenovirus in the transduced cell is selected from a group consisting of E2 and E4; E1, E2 and E4; ~~E2 and E4~~; and E2, E3 and E4.

144. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the foreign gene sequence comprises a 5' portion of the foreign gene sequence.

145. (Previously presented) The adenoviral vector of claim 121 or 122, wherein the foreign gene sequence comprises a 3' portion of the foreign gene sequence.